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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/743,835	12/24/2003	Shiao-Wen Tsai	Q79205	1134

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EXAMINER

LEWIS, PATRICK T

ART UNIT PAPER NUMBER

1623

DATE MAILED: 03/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/743,835

Applicant(s)

TSAI ET AL.

Examiner

Patrick T. Lewis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 30 December 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 12302005.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## DETAILED ACTION

### ***Applicant's Response Dated December 30, 2005***

1. Claims 1-29 are pending. An action on the merits of claims 1-29 is contained herein below.
2. The rejection of claims 1-29 under 35 U.S.C. 112, second paragraph, has been rendered moot in view of applicant's amendment dated December 30, 2005.

### ***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao US 2002/0091251 A1 (Zhao) in combination with Tomihata et al. Journal of Biomedical Materials Research (1997), Vol. 37, pages 243-251 (Tomihata).

Claims 1-28 are drawn to a method for producing double-crosslinked hyaluronate material comprising the steps of: a) subjecting hyaluronic acid or a salt thereof to a first crosslinking reaction using either an epoxide compound or a carbodiimide compound as a crosslinking agent, and b) subjecting the product obtained from step a) to a second crosslinking reaction using the crosslinking agent (an epoxide compound or a carbodiimide compound) not used in step a). Claims 2-3 limit the epoxide compound.

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Claims 4-7 and 9-12 limit the reaction conditions. Claim 8 limits the carbodiimide compound. Claims 13-25 and 28 limit the form of HA. Claims 26-27 further delimit a washing and drying step c). Claim 29 is drawn to a double-crosslinked hyaluronate material produced by the method of claim 1.

Zhoa teaches that hyaluronic acid may be cross-linked by two different types of cross-linking bonds, to effect a 'double cross-linking' (pages 1-2). The formation of different types of bonds is achieved by effecting the cross-linking via different functional groups. The functional groups which are mainly responsible for cross-linking of HA molecules are the hydroxyl and carboxyl groups. Hydroxyl groups may be cross-linked via an ether linkage and carboxyl groups via an ester linkage. Cross-linking agents which may be used in the process include those well-known in the art, including carbodiimide, ethylene glycol polyglycidylether, butanediol diglycidylether, polyglycerol polyglycidylether, polypropylene glycol diglycidylether, or a bis- or poly-epoxy cross-linker such as 1,2,3,4-diepoxybutane or 1,2,7,8-diepoxyoctane. Those skilled in the art will readily be able to select an appropriate cross-linking agent and the appropriate reaction conditions to form the desired bond. The ratio of cross-linking agent to HA employed at each stage of this process will generally be in the range 1:10 to 10:1 by weight (page 3). The individual cross-linking reactions may be carried out according to methods known generally in the art. Thus, the HA utilized as the starting material may be in the form of a film or in solution. The reaction may be effected at a temperature in the range of 15 to 50 C. The time for completion of the cross-linking reaction may in general vary from about an hour to a few days. The precise nature of the product may

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be varied by appropriate selection of reaction conditions so as to control the degree of cross-linking and hence the properties of the product. Factors which influence the degree of crosslinking and hence the nature of the final product include the form of the HA starting material employed, the feeding ratio of crosslinking agent to HA starting material employed, the reaction time, temperature and pH. Whichever cross-linking method is used, the completion of the reaction can be routinely controlled by methods well known in the art, for example, the reaction may be terminated by neutralizing the reaction mixture and solvent precipitation to obtain a product with the desired degree of cross-linking. The final product may be isolated from the reaction medium by conventional procedures.

Zhoa differs from the instantly claimed invention in that Zhoa does not explicitly teach using a combination of an epoxide compound and a carbodiimide compound as the crosslinking agents and does not recite the specific carbodiimide compounds employed; however, these deficiencies would have been obvious to one of ordinary skill in the art at the time of the invention in view of the teachings of Tomihata.

Tomihata teaches the use of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide for making cross-linked hyaluronic acid materials (page 244).

It would have been obvious to one of ordinary skill in the art at the time of the invention to select an epoxide compound and a carbodiimide compound as the crosslinking agents as Zhoa expressly teaches that those skilled in the art would readily be able to select an appropriate cross-linking agent and the appropriate reaction conditions to form the desired bond (paragraph 27). It would have also been obvious to

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one of ordinary skill in the art at the time of the invention to use one of the specific carbodiimide compounds recited in claim 8 such as 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide since it was known in the art for being useful for crosslinking hyaluronic acid. One would have been motivated to do so in order to improve the biostability of HA.

### ***Conclusion***

5. Claims 1-29 are pending. Claims 1-29 are rejected. No claims are allowed.
6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

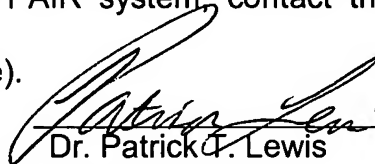
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

**Contacts**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Dr. Patrick T. Lewis  
Primary Examiner  
Art Unit 1623

ptl